

Vasculitis

Inflammation of blood vessels

- There are many different vasculitides.
- May be categorized by size of blood vessel affected.
- e.g. Behcet's disease – affects blood vessels of any size.
- e.g. Giant cell arteritis – affects large blood vessels.
- e.g. Polyarteritis nodosa (PAN) – affects medium blood vessels.
- may be ANCA-positive.
- e.g. Wegener's granulomatosis – affects small blood vessels.

Immunology investigations for vasculitis:

1. **Complement C3 and C4** – low C4 in immune complex disease
2. **Antinuclear antibodies (ANA)**
3. **Anti-neutrophil cytoplasmic antibodies (ANCA)**

Goodpasture's disease

- A **RARE** autoimmune disease caused by antibodies to Type IV collagen present in the glomerular and alveolar basement membranes (**Type II hypersensitivity**).
- Typically have rapidly progressive glomerulonephritis and pulmonary haemorrhage.
- Requires prompt diagnosis and rapid treatment with plasma exchange and immunosuppression, continued until GBMA are undetectable.

GBMA

(Anti-glomerular basement membrane antibodies)

- **URGENT TEST – same day and phone results to clinician.**
- GBMA are pathogenic i.e. cause the disease – most autoantibodies are not pathogenic.
- Test for GBMA by ELISA and if positive, confirm specificity by indirect immunofluorescence on monkey kidney sections. Positive results are phoned to the clinician.
- Anti-GBM antibodies are vital for **diagnosis**, and important for **monitoring** response to treatment.

- Paraproteins and especially monoclonal light chains (Bence Jones protein) can deposit in the kidneys (as myeloma casts or amyloid) and cause renal impairment PLUS hypercalcaemia, raised uric acid, dehydration.

- Free light chains are usually reabsorbed in the proximal tubule but when there is excessive light chains e.g. with monoclonal proteins such as BJP, this mechanism is overwhelmed and the excess light chains can cause renal impairment.
- BJP may form AL amyloid, which is deposited in the kidney causing renal failure (see B cell malignancy poster).

C3 nephritic factor

- An antibody that stabilizes the C3 convertase complex of the alternative complement pathway (activated by pathogen surfaces).
- Causes excessive activation of C3, resulting in low serum C3 concentration.
- Causes membranoproliferative disease with renal impairment.
- Associated with bacterial infection e.g. streptococcus, staphylococcus.

Bence Jones protein (Monoclonal immunoglobulin light chains)

ANCA-associated vasculitides

- All associated with pulmonary and renal symptoms
e.g. haemoptysis, acute renal failure.
Risk of pulmonary haemorrhage.
- Try to diagnose and treat rapidly to limit organ damage.

Churg Strauss Syndrome

- Milder, has allergy prodrome and eosinophilia.
- Associated with P-ANCA and anti-myeloperoxidase antibodies.

Wegener's granulomatosis

- Granulomas, erosive sinus disease.
- Associated with c-ANCA and anti-proteinase 3 antibodies.

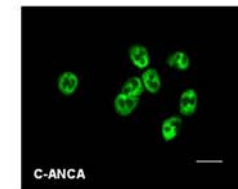
Microscopic polyangiitis

- Rapidly progressive renal failure.
- Associated with P-ANCA and anti-myeloperoxidase antibodies.

ANCA

(Anti-neutrophil cytoplasmic antibodies)

- Screen for ANCA by indirect immunofluorescence on human neutrophils.
- Look for perinuclear (P-ANCA) or cytoplasmic (C-ANCA) staining pattern.
- Follow up with ELISAs for antibodies to myeloperoxidase (MPO, usually P-ANCA pattern) and proteinase-3 (PR3, usually C-ANCA pattern).
- **URGENT TEST – same day and phone results to clinician.**



ANCA staining patterns
Indirect immunofluorescence on human neutrophils showing C-ANCA (cytoplasmic) staining pattern. For P-ANCA (perinuclear) staining pattern, visit the website of the Clinical Immunology Department in Birmingham.
<http://medweb4.bham.ac.uk/websites/clinicalimmunology/index.asp>

RENAL DISEASE

Cryoglobulinaemia

Presence of immunoglobulin that precipitates in the laboratory when incubated at 4C and dissolves when returned to 37C

Type I cryoglobulin

Consists of a monoclonal IgM paraprotein – see B cell malignancy poster.
Symptoms are due to cryoglobulin forming in vivo.

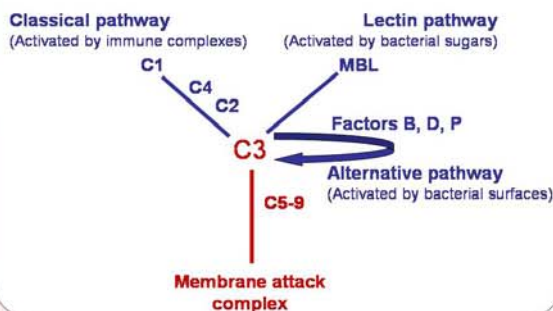
Type II and Type III (mixed) cryoglobulins

- Consist of a monoclonal (Type II) or polyclonal (Type III) rheumatoid factor that forms immune complexes with IgG.
- These immune complexes may be deposited in blood vessel walls, particularly small blood vessels, causing vasculitis. This can cause renal impairment.
- Associated with hepatitis B and hepatitis C viruses.
- Correct collection of cryoglobulins is **ESSENTIAL** for correct results.
- Typical laboratory results are:
 - Presence of a cryoprecipitate in samples stored at 4C.
 - Low C4 concentration, due to immune complexes activating classical complement pathway.
 - Positive rheumatoid factor.



Type II (mixed) cryoglobulin

Complement cascade



Rheumatological disease + renal failure

- Lupus nephritis** – associated with antinuclear antibodies.
- Scleroderma renal crisis** – Occurs in systemic sclerosis, associated with anti-RNA polymerase antibodies. Very rare.
See Rheumatology poster.